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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/367,859	09/02/1999	JAMES SAMSOONDAR	5352-051	4860

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Schwegman, Lundberg, Woessner & Kluth, P.A.
P.O. Box 2938
Minneapolis, MN 55402

EXAMINER
SODERQUIST, ARLEN

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/367,859	SAMSOONDAR, JAMES	
	Examiner	Art Unit	
	Arlen Soderquist	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,10-12,23-25,27,29 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,10-12,23-25,27,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 8, 10-12, 23-25, 27 and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis in view of Sagusa, Gimpel, Simon and Christenson, Leissing or Mullins. In the patent Davis teaches a method of detecting hemolysis in a whole-blood sample, a method of determining an elevation in the potassium ion concentration of a whole-blood sample, an apparatus for detecting hemolysis and/or determining an elevation in the potassium ion concentration in a fluid sample, an apparatus for detecting hemolysis and/or determining an elevation in the potassium ion concentration in a whole-blood sample, and a single-use cartridge containing a plurality of microfabricated biosensors which further contains a hemolysis detection unit. Columns 2-3 of the application teach the interference from hemoglobin caused through hemolysis of red blood cells through both an increase in the concentration of other components found in the red blood cells or through colorimetric interference with chromogenic reagents. In particular column 2 lines 46-52 teaches the prior method of checking the color of the plasma sample for the red coloration associated with the presence of hemolysis. Column 3 lines 12-18 list several analytes which can be affected through the presence of hemolysis including potassium, lactate dehydrogenase, cholesterol, prostatic phosphatase, aspartate aminotransferase, and alanine aminotransferase, aldolase, total acid phosphatase, isocitrate hydrogenase, magnesium and phosphate. Columns 6-8 teach how the presence of hemoglobin is detected with column 8 lines 10-36 being particularly relevant to the instant claims. The section of column 8

teaches the use of a reflectance meter and forming a calibration graph to determine the concentration of hemoglobin present. Column 8-9 teach how the measurement of the hemoglobin concentration is used to correct the analyte measurement. Of particular interest is column 9 lines 44-56 teaching the relationships between hemolyzed red blood cells, the concentration of Hb, and the elevation of blood analytes such as potassium ion concentration are linearly dependent upon each other. As a result, those of ordinary skill in the art will be able to pre-select a value of hemolysis which corresponds to both a known concentration of Hb in plasma and the corresponding color thereof, which in turn correlates to a pre-selected elevation in the potassium ion concentration. Davis does not teach interference by blood substitutes, using derivative spectroscopy in the correction equation or detection of pseudohemolysis.

In the patent Sagusa teaches a colorimetric method for samples including interfering chromogens. Color former is added to blood serum sample color it, and measurements for specific components are determined based on the light absorbance caused by coloring. For one sample, a differential light absorbance between two wavelengths at each of long wavelength region, middle wavelength region and short wavelength region within a visible wavelength band is determined. The degree of chyle is determined from the measurements for the long wavelength region, the degree of hemolysis is determined from the measurements for the middle wavelength region, and the degree of icterus is determined from the measurements for the short wavelength region. The measurements for the specific components are then corrected by the degree of chyle, degree of hemolysis and degree of icterus to obtain highly correct measurements.

In the abstract Christenson discusses hemoglobin based blood substitutes and their interference with routine chemical tests.

In the abstract Leissing discusses modification of clinical chemistry methods to overcome interferences from diaspirin crosslinked hemoglobin (DCLHb).

In the paper Mullins discusses effects of Fluosol-DA (artificial blood) on clinical chemistry tests and instruments. Artificial blood must be added to the list of therapeutic agents that produce interference with diagnostic laboratory tests. Fluosol-DA (Alpha Therapeutic Corp., Los Angeles, CA), a stable 20% emulsion of perfluorocarbons in aqueous medium, is being evaluated in clinical trials as a blood substitute in the United States. They investigated its

effects in blood and serum samples on test results and instruments in the clinical chemistry laboratory. The 20% emulsion was added to blood or serum specimens in amounts corresponding to the replacement of in-vivo plasma volumes of 10-50%, concentrations that would be expected in blood samples obtained from patients who have received Fluosol. Observed interferences mimicked those caused by high triglyceride concentrations in serum specimens: interference with chemical reactions and generation of spurious absorbance readings because of turbidity. These types of errors are often additive, and the cumulative effect may cause either erroneously high or low values for the analytes concerned. Because Fluosol may be used widely, although infrequently, for patients refusing blood transfusions on religious grounds and for patients with rare antibodies to red blood cells who require transfusion, laboratories analyzing specimens containing Fluosol should be aware of the potential errors.

In the paper Gimpel teaches a reference interval for the bilirubin excess in cerebrospinal fluid by derivative spectrophotometry. The value of the bilirubin excess can be a useful aid for recognizing blood from hemorrhage in cerebrospinal fluid. One of the parameters needed for the calculation of the bilirubin excess is the total bilirubin concentration in cerebrospinal fluid. A method for measuring total bilirubin in cerebrospinal fluid is presented, based on diazotization of bilirubin according to Jendrassik-Grof, combined with multiwavelength first-derivative spectrophotometry. This bilirubin assay allows determination of total bilirubin concentrations as low as 0.045 mol/L. This method also enables a correlation for oxyHb interference. The value of the bilirubin excess was calculated for patients not showing any neurological disorder. A reference interval of 0.07 ± 0.06 mol/L was calculated for the bilirubin excess. Particularly relevant to the instant claims is the calculations and equations shown in the right column of page 218.

In the paper Simon discusses a "pseudo-hemolytic" transfusion reaction caused by intravenous iron-dextran therapy. Intravenous iron-dextran therapy can cause a red-brown discoloration of the plasma, simulating a hemolytic transfusion reaction. A rapid and simple test to differentiate between true hemolysis and plasma discoloration due to circulating iron-dextran complexes is described.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include substances such as blood substitutes recognized by Christenson, Leissing or

Mullins as interfering substances into the Davis correction method because of the recognized possibility for interference with clinical chemistry tests and the projected use of these substances in humans. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use different wavelengths as taught in the Sagusa method to differentiate between true hemolysis and plasma discoloration due to circulating colored substances as taught by Simon in the Davis method because of the ability to select wavelengths that will allow the effects of one chromogen to be removed from another chromogen as taught by Sagusa and the need to differentiate between true hemolysis and plasma discoloration due to circulating substances as taught by Simon. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a derivative spectroscopic method as shown by Gimpel for correction in the Davis method because of the ability to differentiate between interfering substances such as the hemoglobin and bilirubin of Gimpel. Determination of specific wavelengths would be a results effective variable which has been held to be within the skill of the routineer in the art by the Courts (see *In re Boesch*, 205 USPQ 215 (CCPA 1980)).

4. Applicant's arguments filed May 19, 2003 have been fully considered but they are not persuasive. The Davis reference clearly deals with correction of analyses in the presence of an interfering substance such as hemoglobin from hemolysis of a blood sample. The language of claim 24 is such that the determination is the presence of hemolysis, pseudohemolysis ***or*** both which is satisfied by determining either or both. Thus the determination of hemolysis satisfies the claim. The presence of substances in the blood (blood substitutes) that would also interfere with an analysis in a manner similar to hemolysis is shown by the secondary references as well as means to remove the influence of the interfering compounds. Thus it would have been obvious to modify the teachings of Davis to include the possibility of pseudohemolysis due to its recognized presence and effects on the analysis of other components of a blood sample. Since the references are dealing with interfering substances in an analysis they are properly combinable. The Courts have recognized that a secondary reference does not need to be physically combinable with the primary reference to render the invention under review obvious. Along these lines applicant is directed to *In re* Sneed 218 USPQ 385, 389 (Fed. Cir. 1983) and *In re* Keller 208 USPQ 871, 880 (CCPA 1981) .

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (703) 308-3989. The examiner's schedule is variable between the hours of about 5:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

For communication by fax to the organization where this application or proceeding is assigned, (703) 305-7719 may be used for official, unofficial or draft papers. When using this number a call to alert the examiner would be appreciated. Numbers for faxing official papers are 703-872-9310 (before finals), 703-872-9311 (after-final), 703-305-7718, 703-305-5408 and 703-305-5433. The above fax numbers will generally allow the papers to be forwarded to the examiner in a timely manner.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

Arlen Soderquist

August 11, 2003

ARLEN SODERQUIST
PRIMARY EXAMINER